First Asymmetric Diels−Alder Reactions of Furan and Chiral Acrylates. Usefulness of Acid Heterogeneous Catalysts

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$TiCl_4$ and $ZnCl_2$ supported on silica gel catalyze the reactions of furan with methyl, (1*R*,2*S*,5*R*)-menthyl, and (1*R*,2*S*,5*R*)-8-phenylmenthyl acrylates. The best results are obtained when reactions are carried out without a solvent. The *endo*/*exo* and diastereofacial selectivities depend on the nature of the catalyst and on the reaction conditions. With the (1*R*,2*S*,5*R*)-menthyl acrylate 44% de in *endo* cycloadducts and 20% de in *exo* cycloadducts are the best asymmetric inductions. With the (1*R*,2*S*,5*R*)-8-phenylmenthyl acrylate 68% de in *endo* and 70% de in *exo* cycloadducts are obtained.

Introduction

2-Substituted 7-oxabicyclo[2.2.1]hept-5-ene derivatives are powerful intermediates in the preparation of carbohydrates and other biologically active compounds.[1−4] These products can be obtained, via Diels−Alder reactions, from furan, an inexpensive compound obtained from agricultural leftovers.[5] Given their relationship with biologically active compounds, there is a noticeable interest in the asymmetric preparation of these bicyclic compounds and excellent results have been described[6] using chiral derivatives of acrylonitrile, such as 1-(cyanovinyl)-(1′*S*)-camphanate, as a chiral dienophile. More recently chiral 2-siloxyfurans have been used as chiral dienes, with $Eu(hfc)_3$ as a chiral catalyst.[7] However, there is no method for obtaining 7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylates in an asymmetric way. This fact is surprising because the racemic compounds have gained interest as synthetic intermediates[3] and because the use of chiral acrylates is the most widely used methodology to carry out asymmetric Diels−Alder reactions.[8]

The lack of references about reactions of chiral acrylates with furan is undoubtedly due to the difficulties related to the use of furan as a diene. Furan is an acid-sensitive reagent and cannot be used in the presence of the most common Lewis acids. Heating is often an ineffective alternative because the cycloadducts are thermally unstable and easily revert to the reagents or are cleaved into 2-substituted furans. Furthermore the use of an excess of diene leads to the formation of byproducts and the instability of the cycloadducts makes the purification difficult. Several methods have been developed to carry out reactions of furan with nonchiral acrylates, such as using very long reaction times,[9] high pressure,[10,11] ZnI_2 at 40 °C in sealed tubes,[12] cupric fluoroborate in the presence of hydroquinone and long reaction times,[13] and Y zeolites.[14] However, 79% is the maximum yield obtained with methyl acrylate at room temperature and 20 000 atm.[10] The situation with chiral acrylates is even worse given that the Diels−Alder reactivity of acrylates with furan decreases as the size of the alcohol increases.[11] Finally, the induction of asymmetry with chiral acrylates is based on the kinetic control of the Diels−Alder reaction and the easy reversibility observed when furan is used as a diene may have a nonpredictable effect on the diastereofacial selectivity. To sum up, the development of a method to carry out reactions of furan with chiral acrylates with good yields and selectivities is a very interesting yet difficult task.

We have shown that several Lewis acids supported on silica gel are useful catalysts in Diels−Alder reactions of nonchiral[15,16] and chiral[16] α,β-unsaturated esters. Furthermore, some of these supported Lewis acids improve the selectivity, with regard to side reactions, when used in the absence of a solvent. For instance, they promote Diels−Alder reactions of nonchiral[17] and chiral[18] (*E*)-2-phenyl-5(4*H*)-oxazolones without causing *E*/*Z* isomerization.

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Scheme 1

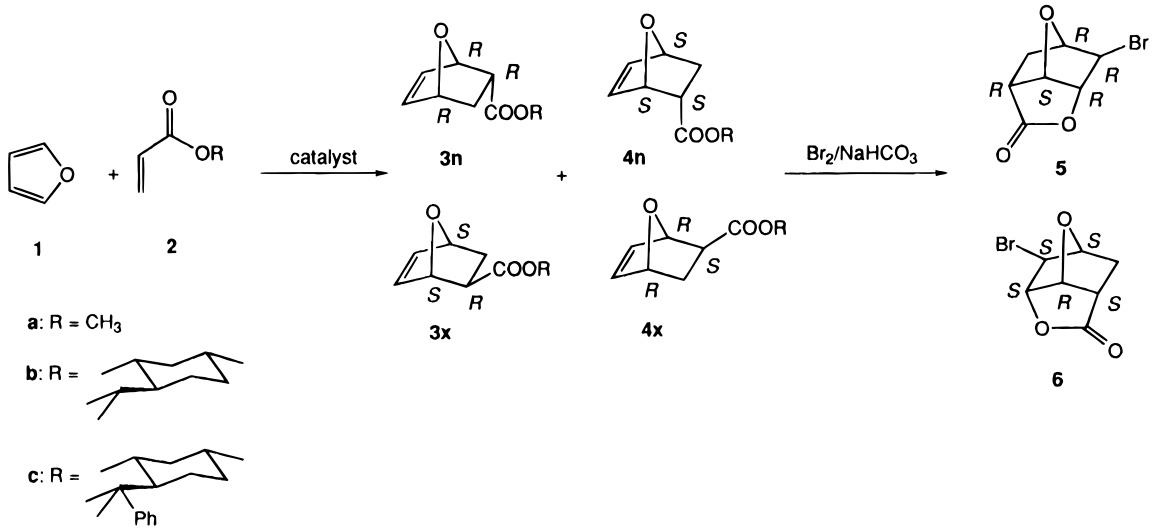

Table 1. Results Obtained in the Reaction of Furan (1) with Methyl Acrylate (2a) after 24 h at 25 °C

catalyst	**1**:**2a**	solvent	% conversion[a]	endo/exo[a,b]
SiO_2	6:1	$CDCl_3$	0	
	6:1		8	
SiO_2−Al	6:1	$CDCl_3$	3	
	6:1		51	60:40
SiO_2−Ti	6:1	$CDCl_3$	35	77:23
	6:1		71	73:27
	3:1		52	50:50
SiO_2−Zn	6:1	$CDCl_3$	16	79:21
	6:1		75	81:19
	3:1		22	86:14

[a] Determined by ^{1}H-NMR. [b] Assigned on the basis of previously described spectra (ref 9).

In view of this we have tested these supported Lewis acids as catalysts in the reaction of furan (**1**) with methyl, (1*R*,2*S*,5*R*)-menthyl, and (1*R*,2*S*,5*R*)-8-phenylmenthyl acrylates (**2a**, **2b**, and **2c**, respectively) (Scheme 1).

Results and Discussion

SiO_2−Al and SiO_2−Ti were obtained by reaction of silica gel (Merck, silica gel 60, 63−200 nm) with Et_2AlCl and $TiCl_4$ following the previously described method.[15] SiO_2−Zn was obtained from $ZnCl_2$ and silica gel (EP11 from Crossfield) as previously described.[19] The catalytic activity of these solids, together with that of silica gel 60 from Merck, was compared in the reaction of furan (**1**) with methyl acrylate (**2a**). The results obtained (Table 1) show that silica gel does not catalyze this reaction, whereas the treated silicas do. Supported $TiCl_4$ and $ZnCl_2$ are more efficient than supported Et_2AlCl. The best chemical yields are obtained when the reactions are carried out without a solvent and the *endo*/*exo* selectivity depends on the catalyst, on the proportion of reagents, and on the presence or absence of solvent. The influence of the solvent on the *endo*/*exo* selectivity of Diels−Alder reactions of furan has been also detected in reactions carried out at high pressure.[20]

The same solids were tested as catalysts in the reaction between furan (**1**) and (1*R*,2*S*,5*R*)-menthyl acrylate (**2b**) (Table 2). The *endo* and *exo* cycloadducts were assigned

Table 2. Results Obtained in the Reaction of Furan (1) with the Chiral Acrylates 2b and 2c at 25 °C

dieno-phile	catalyst	**1**:**2**	solvent	time (h)	% conv	endo/ exo[a]	% de[a] endo[b]	% de[a] exo[b]
2b	SiO_2	10:1	CH_2Cl_2	3	0			
		10:1		3	0			
	SiO_2−Al	10:1	CH_2Cl_2	3	0			
		10:1		3	15	50:50	46	10
	SiO_2−Ti	10:1	CH_2Cl_2	3	34	66:34	32	10
		10:1		3	82	62:38	44	10
		6:1		3	37	57:43	38	9
		6:1		24	48	55:45	43	20
		3:1		24	30	76:24	20	8
	SiO_2−Zn	10:1	CH_2Cl_2	3	10	68:32	44	10
		10:1		3	58	50:50	32	9
		6:1		3	52	55:45	36	19
		6:1		24	57	50:50	10	10
		3:1		24	47	50:50	26	8
2c	SiO_2−Ti	10:1		3	26	31:69		
		10:1		24	79	33:67	33	70
	SiO_2−Zn	10:1		3	17	60:40		
		10:1		24	46	50:50	68	66

[a] Determined by ^{1}H- and ^{13}C-NMR. [b] **3n** and **3x** are the major cycloadducts.

on the basis of their ^{1}H- and ^{13}C-NMR spectra. As in the adducts obtained from methyl acrylate, the signal corresponding to H_2 appears at a higher chemical shift in the *endo* cycloadducts (**3nb** + **4nb**, 3.07 ppm) than in the *exo* (**3xb** + **4xb**, 2.42 ppm). The position of the carbonyl carbons in ^{13}C-NMR agrees with this assignment because in the *endo* isomers (**3nb** + **4nb**) this carbon is shielded by the double bond and appears at a higher field (171.7 ppm) than in the *exo* isomers (**3xb** + **4xb**, 173.2 ppm). The percentage of conversion and the different selectivities were detemined by ^{13}C-NMR of the vinyl carbons [**2b**, 129.0 ppm (C_α), 130.1 ppm (C_β); **3nb** 132.3 ppm (C_6); **4nb**, 132.6 ppm (C_6); **4xb**, 134.7 ppm (C_6); **3xb**, 134.8 ppm (C_6)].

The cycloadducts cannot be purified by chromatography on silica gel because they decompose. This is probably due to the acidity of the silica gel, located in the free hydroxyl groups of the surface. If this interpretation is correct, a possible solution to this problem would be to eliminate most of this acidity through an "end-capping" procedure. This was effectively carried out by treatment of the silica gel with hexamethyldisilazane (HMDS). With this in-house stationary phase, we were able to successfully separate the *endo* (**3nb** + **4nb**) and

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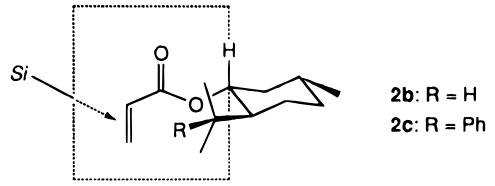

Figure 1. Model to account for the direction of the asymmetric induction experimentally observed.

exo (**3xb** + **4xb**) cycloadducts by column chromatography using hexane/diethyl ether (100:1) as an eluent.

In order to determine the absolute configuration of the major *endo* cycloadduct, the mixture coming from a reaction (SiO_2−Ti, no solvent, 3 h, 10-fold excess of furan) was treated with bromine and aqueous sodium hydrogen carbonate. The mixture of bromo lactones (**5** + **6**) was also purified by column chromatography on "end-capped" silica gel, using hexane/diethyl ether, initially with 100:1 and then with 1:1, as an eluent, followed by recrystallization from ethyl acetate. The polarimetric analysis of this product gives an $[\alpha]_D^{25} = -50°$ (*c* 0.99 in $CHCl_3$). A comparison of this value with that previously described[21] indicates that **5** is the major bromolactone with 54% ee. It is important to note that in the purification process an increase of the ee with regard to that determined in the crude of the reaction is observed, so that the ee determined after this purification step cannot be taken in general as a measure of the asymmetric induction produced in the reaction.

The formation of **3nb** as a major cycloadduct can be explained by the model used in Lewis acid-catalyzed reactions of the same dienophile **2b** with cyclopentadiene.[8] In this model the dienophile displays an *anti* enoate conformation where the isopropyl group of the chiral auxiliary shields the *Re* face of the dienophile and the attack of the diene preferentially takes place on the *Si* face (Figure 1). On the basis of this model **3xb** was assigned as the major *exo* cycloadduct.

Table 2 summarizes the results obtained from the reaction of furan (**1**) and (1*R*,2*S*,5*R*)-menthyl acrylate (**2b**). Silica gel and silica gel treated with Et_2AlCl are not good catalysts for this reaction. The best results are again obtained when the reactions are carried out in the absence of a solvent. The use of long reaction times does not noticeably improve the conversion but the selectivity tends to decrease. Therefore the best results are obtained by using a large excess of diene with short reaction times. Under these conditions, the silica modified by treatment with $TiCl_4$ provides the best results. It is important to note that the asymmetric induction obtained in the *endo* cycloadducts is comparable to that described for the reaction of this dienophile with cyclopentadiene.[16a]

The best catalysts, namely SiO_2−Ti and SiO_2−Zn, were tested in the reaction between (1*R*,2*S*,5*R*)-8-phenylmenthyl acrylate (**2c**) and furan (**1**) in the absence of a solvent (Table 2). The *endo* and *exo* cycloadducts were again assigned by the higher chemical shift of H_2 in the *endo* (**4nc**, 2.27 ppm; **3nc**, 2.50 ppm) than in the *exo* (**3xc** + **4xc**, 1.55−1.70 ppm) and by the lower chemical shift of the carbonyl carbon in the *endo* (**4nc**, 171.2 ppm; **3nc**, 171.6 ppm) than in the *exo* cycloadducts (**3xc** + **4xc**, 173.2 ppm). The percentage of conversion and the selectivities were determined by ^{13}C-NMR of the vinyl carbons [**2c**, 129.8 ppm (C_α+C_β); **3nc** 133.1 ppm (C_6); **4nc**, 132.1 ppm (C_6); **3xc** + **4xc**, 134.5 ppm (C_6)] and by ^{1}H-NMR of the vinyl protons (**2c**, 5.75, 5.95, 6.08 ppm ($3H_{vinyl}$); **3nc** + **4nc**, 6.35 ppm (H_6); **4xc** 6.30 ppm (H_6); **3xc**, 6.25 ppm (H_6); **3nc** + **3xc**, 6.20 ppm (H_5); **4nc**, 6.01 ppm (H_5); **4xc**, 6.12 ppm (H_5)].

Endo (**3nc** + **4nc**) and *exo* (**3xc** + **4xc**) cycloadducts were separated by column chromatography on "end-capped" silica gel using hexane/diethyl ether (100:1) as an eluent. In this way the major *exo* cycloadduct (**3xc**) was obtained in pure form.

A mixture of bromo lactones (**5** + **6**) was obtained, as described above, from the reaction carried out with SiO_2−Zn. The mixture obtained gave $[\alpha]_D^{25} = -70.3°$ (*c* 0.99 in $CHCl_3$), indicating that **3nc** is the major *endo* cycloadduct. This value correponds to 76% ee, so the purification process increases the amount of the major enantiomer. This result can be accounted for by the classical model used in Lewis acid-catalyzed reactions of this dienophile[8] (Figure 1), and **3xc** was assigned as the major *exo* cycloadduct on the basis of this model.

The results obtained (Table 2) show that $TiCl_4$ supported on silica gel (SiO_2−Ti) is more efficient than SiO_2−Zn. In contrast to that observed in the reaction of (1*R*,2*S*,5*R*)-menthyl acrylate (**2b**), the use of SiO_2−Ti leads to a preference of the *exo* cycloadducts and furthermore the diastereofacial selectivity in *exo* cycloadducts is 70% de. The reaction carried out with SiO_2−Zn showed little or no *endo*/*exo* selectivity, but the diastereofacial selectivity was about the same (67% de) in *endo* and *exo* cycloadducts.

Conclusion

It can be concluded that $ZnCl_2$ and $TiCl_4$ supported on silica gel are fairly efficient catalysts for the reactions of chiral acrylates with furan. The second catalyst leads to the best percent conversion, but the *endo*/*exo* and diastereofacial selectivities depend on the nature of the catalyst and the chiral auxiliary. The best results are obtained in reactions carried out in the absence of a solvent. The purification of the products allows the major *exo* cycloadduct (**3xc**) in pure form and the bromo lactone with 76% ee to be obtained, and furthermore this enantiomeric excess can be further improved by recrystallization. The synthetic methodology described here is capable of being used in the preparation of furan derivatives in enantiomerically pure form, which are of interest as intermediates in the synthesis of biologically active compounds. These studies are in progress and will be reported in due course.

Experimental Section

(1*R*,2*S*,5*R*)-Menthyl and (1*R*,2*S*,5*R*)-8-phenylmenthyl acrylates were prepared according to a procedure described in the literature.[22] Silica-supported $AlEt_2Cl$ and $TiCl_4$ were prepared from Merck silica gel 60 as previously described.[15] $ZnCl_2$ was supported on EP11 silica from Crossfield following a previously described procedure.[19] The silicas contained 1.4 mmol of Al g^{-1}, 1.2 mmol of Ti g^{-1}, and 1.5 mmol of Zn g^{-1}, respectively.

Diels−Alder Reactions in Solution. Under argon, 1 mmol of the dienophile (**2a** or **2b**) and the corresponding amount of freshly distilled furan (6 mmol for **2a** and 10 mmol for **2b**) were added to a suspension of the catalyst (1 g) in 6 mL of the solvent ($CDCl_3$ for **2a** and CH_2Cl_2 for **2b**). The

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reactions were shaken for the time indicated (Tables 1 and 2). For the reactions of **2a** the solution was extracted from the reaction flask with a syringe and directly analyzed by ^{1}H-NMR. For the reactions of **2b** the catalyst was separated by filtration and washed with CH_2Cl_2. The solvent was eliminated under reduced pressure and the crude reactions were analyzed by ^{1}H- and ^{13}C-NMR in $CDCl_3$. The conversion and selectivities were determined by integration of the signals given in the text.

Diels−Alder Reactions in the Absence of a Solvent. Under argon, 1 mmol of the dienophile (**2a**, **2b**, or **2c**) and the corresponding amount of freshly distilled furan (Tables 1 and 2) were added to 1 g of the catalyst. The reactions were stirred for the time indicated (Tables 1 and 2). For the reactions of **2a**, 6 mL of $CDCl_3$ were added, and the solution was extracted with a syringe and analyzed by ^{1}H-NMR. For the reactions of **2b** and **2c**, 6 mL of CH_2Cl_2 were added, and the catalyst was separated by filtration and thoroughly washed with CH_2Cl_2. The solvent was eliminated under reduced pressure and the crude reactions were analyzed by ^{1}H- and ^{13}C-NMR in $CDCl_3$. The conversion and selectivities were determined by integration of the signals given in the text.

End-Capping of the Silica Gel. From a suspension of silica gel (100 g) in toluene (400 mL), a mixture of toluene and water (100 mL) was distilled. Then 50 mL of hexamethyldisilazane (HMDS) were added, and the mixture was heated under reflux for 45 min. After this time, the solid was separated by filtration and thoroughly washed with diethyl ether, ethanol, and diethyl ether and then dried under vacuum. This solid was used in the chromatographic purification of the cycloadducts.

(1*R*,2*S*,5*R*)-Menthyl (1*R*,2*R*,4*R*)- and (1*S*,2*S*,4*S*)-7-Oxabicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylates (3nb + 4nb). These products were separated from the reaction mixture by column chromatography using the "end-capped" silica gel and hexane/diethyl ether (100:1) as an eluent. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 6.42 (dd, J = 5.7, 1.8 Hz), 6.20 (dd, J = 5.7, 1.8 Hz), 6.15 (dd, J = 5.7, 1.5 Hz), 5.15 (m), 5.01 (m), 4.60 (m), 3.07 (m), 2.12−2.02 (m), 1.95−1.85 (m), 1.85−1.75 (m), 1.7−1.6 (m), 1.55 (m), 1.5−1.3 (m), 1.1−0.9 (m), 0.85 (m), 0.7 (m). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 171.7, 137.2, 137.0, 132.6, 132.3, 79.0, 78.9, 74.6, 46.9, 43.1, 40.8, 34.2, 31.3, 28.2, 26.1, 23.1, 22.0, 20.8, 15.9. Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.35; H, 9.32. Found C, 73.29; H, 9.20.

(1*R*,2*S*,5*R*)-Menthyl (1*S*,2*R*,4*S*)- and (1*R*,2*S*,4*R*)-7-Oxabicyclo[2.2.1]hept-5-ene-2-*exo*-carboxylates (3xb + 4xb). These products were separated from the reaction mixture as described above. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 6.38 (m), 5.15 (m), 5.05 (m), 4.71 (m), 2.42 (m), 2.2−2.1 (m), 2.05−1.95 (m), 1.9−1.8 (m), 1.7−1.6 (m), 1.5−1.3 (m), 1.1−0.9 (m), 0.85 (m), 0.7 (m). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 173.2, 137.0, 137.0, 134.8, 134.7, 81.1, 78.0, 74.6, 47.0, 43.1, 40.8, 34.2, 31.3, 29.0, 26.2, 23.3, 22.0, 20.8, 16.1. Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.35; H, 9.32. Found C, 73.18; H, 9.60.

(1*R*,2*S*,5*R*)-8-Phenylmenthyl (1*R*,2*R*,4*R*)- and (1*S*,2*S*,4*S*)-7-Oxabicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylates (3nc + 4nc). These products were separated from the reaction mixture by the same chromatographic method described above for the cycloadducts obtained from **2b**. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 7.3−7.2 (m), 7.2−7.1 (m), 6.35 (dd, J = 5.7, 1.8 Hz), 6.20 (dd, J = 6.1, 1.6 Hz), 6.01 (dd, J = 5.7, 1.6 Hz), 4.92 (m), 4.85 (m), 4.72 (m), 4.50 (m), 2.50 (m), 2.27 (m), 2.05−1.95 (m), 1.9−1.8 (m), 1.7−1.55 (m), 1.45−1.35 (m), 1.30 (s), 1.21 (m), 1.19 (s), 1.1−0.9 (m), 0.8 (d). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 171.6, 171.2, 151.5, 136.4, 133.1, 132.1, 127.9, 125.3, 125.1, 78.7, 78.6, 74.5, 50.0, 43.0, 41.6, 39.6, 34.4, 31.2, 29.2, 26.5, 24.7, 23.3, 21.7. Anal. Calcd for $C_{23}H_{30}O_3$: C, 77.93; H, 8.65. Found C, 78.10; H, 8.66.

(1*R*,2*S*,5*R*)-8-Phenylmenthyl (1*S*,2*R*,4*S*)-7-Oxabicyclo[2.2.1]hept-5-ene-2-*exo*-carboxylate (3xc). This product was separated from the reaction mixture as described above. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 7.3−7.2 (m, 3H), 7.2−7.1 (m, 2H), 6.25 (dd, J = 6.1, 1.6 Hz, 1H), 6.20 (dd, J = 6.1, 1.6 Hz, 1H), 4.95 (m, 1H), 4.90 (m, 1H), 4.85 (m, 1H), 2.01 (m, 1H), 1.82 (m, 1H), 1.70−1.55 (m, 4H), 1.5−1.4 (m, 1H), 1.23 (s, 3H), 1.20 (m, 1H), 1.15 (s, 3H), 1.15−0.9 (m, 3H), 0.85 (d, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 173.2, 151.8, 136.6, 134.5, 127.8, 125.4, 124.9, 80.0, 77.1, 74.4, 50.0, 42.2, 41.6, 39.6, 34.5, 31.2, 29.4, 28.4, 26.4, 24.5, 21.7. Anal. Calcd for $C_{23}H_{30}O_3$: C, 77.93; H, 8.65. Found C, 77.78; H, 8.79.

(1*R*,2*S*,5*R*)-8-Phenylmenthyl (1*R*,2*S*,4*R*)-7-Oxabicyclo[2.2.1]hept-5-ene-2-*exo*-carboxylate (4xc). The data of this product were obtained from a mixture of **3xc** and **4xc**. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 7.3−7.2 (m, 3H), 7.2−7.1 (m, 2H), 6.30 (dd, J = 5.9, 1.7 Hz, 1H), 6.12 (dd, J = 5.9, 1.7 Hz, 1H), 4.95 (m, 1H), 4.85 (m, 1H), 4.58 (m, 1H), 2.01 (m, 1H), 1.82 (m, 1H), 1.70−1.55 (m, 4H), 1.5−1.4 (m, 1H), 1.23 (s, 3H), 1.20 (m, 1H), 1.15 (s, 3H), 1.15−0.9 (m, 3H), 0.85 (d, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 173.2, 151.8, 136.6, 134.5, 127.8, 125.4, 124.9, 80.0, 77.1, 74.4, 50.0, 42.2, 41.6, 39.6, 34.5, 31.2, 29.4, 28.4, 26.4, 24.5, 21.7. Anal. Calcd for $C_{23}H_{30}O_3$: C, 77.93; H, 8.65. Found C, 77.89; H, 8.74.

(1*R*,2*R*,3*R*,6*R*,7*S*)- and (1*S*,2*S*,3*S*,6*S*,7*R*)-2-Bromo-4,8-dioxatricyclo[4.2.1.0^{3,7}]nonan-5-one (5 + 6). The crude obtained from a reaction of **2b** or **2c** was stirred with a solution of $NaHCO_3$ (1.6 mmol) and Br_2 (2.4 mmol) in water (3 mL) for 1 h at room temperature. After this time the aqueous solution was extracted with ethyl acetate, the organic phase was washed with a saturated solution of $Na_2S_2O_3$ and dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The oil obtained was purified by column chromatography using "end-capped" silica gel as a stationary phase and hexane/diethyl ether (initially with 100:1 and then with 1:1) as an eluent. The different fractions obtained were monitored by gas chromatography (FID detector on a Hewlett-Packard 5890II, cross-linked methyl silicone column 25 m × 0.2 mm × 0.33 μm, helium as carrier gas, 20 psi, injector temperature 230 °C, detector temperature 250 °C, oven temperature program 100 °C (2 min)−25 °C/min−220 °C (5 min), retention times: (−)-menthol 5.4 min, bromolactone 7.6 min, (−)-8-phenylmenthol 10.5 min). In this way the bromo lactone was separated and the chiral auxiliaries were recovered. The bromo lactone was further purified by recrystallization from ethyl acetate. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 5.41 (t, J = 4.8 Hz), 4.95 (d, J = 4.8 Hz), 4.75 (d, J = 5.1 Hz), 3.92 (s), 2.75 (m), 2.30 (m), 2.09 (dd, J = 13.5, 1.8 Hz). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 175.8, 86.1, 83.0, 81.5, 50.3, 38.2, 35.6. Anal. Calcd for $C_7H_7BrO_3$: C, 38.39; H, 3.22. Found C, 38.18; H, 3.10.

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Supporting Information Available: A full listing of ^{1}H- and ^{13}C-NMR data of compounds **3nb** + **4nb**, **3xb** + **4xb**, **3nc** + **4nc**, **3xc**, **4xc**, and **5** + **6**, complete with peak assignments (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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